

ON THE MEDICAL ACTIVITY OF THE HEMP PLANT, AS GROWN IN NORTH AMERICA.

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Almost from time immemorial various preparations of the hemp plant have been used in India for the production of a peculiar intoxication. These, or allied preparations have also in modern times been largely used in medicine. It has been thought by some that the hemp of India is specifically distinct from the European plant, but there are really no specific differences, the former differing from the latter only in minor particulars, such as size, the results of the modifying influences of soil and climate. As the drug has become an important article of commerce, attempts have been made to obtain the medicinal principle, a peculiar resinoid body, from plants grown in Great Britain, by which it has been determined that although the resin does exist in such plants, yet it is in so small quantity, that they are not available for manufacturing purposes. The summers of England appear to be too cool to enable the hemp to elaborate its peculiar resin in any quantity. The world has, therefore, been dependent upon India for its supplies of this widely used narcotic. The plants with which the following experiments were made, were raised in the vicinity of Lexington, Kentucky. They were male plants, which had been grown for the purpose of fertilizing seeding female plants, and which having fulfilled that office, were of no further value to the cultivator. They were obtained for me, by R. B. Hamilton, Esq. of Lexington, to whom my thanks are due for the trouble taken by him to aid my investigation.

The first experiment was as follows: an ounce and a half of the powdered leaves, were treated with hot alcohol, although not to exhaustion. The tincture thus made was evaporated and an alcoholic extract obtained. About 4½ P. M., Sept. 23d, I took most of this extract, in a lump, which a druggist estimated to contain from 20 to 30 grains. No immediate symptoms were produced. About 7 P. M., a professional call was requested and forgetting all about the hemp, I went out and saw my patient. Whilst writing the prescription, I became perfectly oblivious to surrounding objects but went on writing, without any check to or deviation from the ordinary series of mental acts, connected with the process, at least that I am aware of. When the recipe was finished, I suddenly recollected where I was, and looking up, saw my patient sitting quietly before me. The conviction was irresistible, that I had sat thus many minutes, perhaps hours, and directly, the idea fastened itself that the hemp had commenced to act, and had thrown me into a trance-like state of considerable duration, during which I had been stupidly sitting before my wondering patient.

I hastily arose and apologized for remaining so long, but was assured

I had only been a very few minutes. About 7½ p. m. I returned home. I was by this time quite excited, and the feeling of hilarity now rapidly increased. It was not a sensuous feeling, in the ordinary meaning of the term; it was not merely an intellectual excitation, it was a sort of *bien-être* — the very opposite to *malaise*. It did not come from without; it was not connected with any passion or sense. It was simply a feeling of inner joyousness; the heart seemed buoyant beyond all trouble; the whole system felt as though all sense of fatigue were forever banished; the mind gladly ran riot, free constantly to leap from one idea to another, apparently unbound from its ordinary laws. I was disposed to laugh; to make comic gestures—one very frequently recurrent fancy, was to imitate with the arms the motions of a fiddler, and with the lips the tune he was supposed to be playing. There was nothing like wild delirium, nor any hallucinations that I remember. At no time had I any visions, or at least any that I can now call to mind; but a person, who was with me at that time, states that once I raised my head and exclaimed, “Oh, the mountains! the mountains!” Whilst I was performing the various antics, already alluded to, I knew very well I was acting exceedingly foolishly but could not control myself.

I think it was about 8 o'clock, when I began to have a feeling of numbness in my limbs, also a sense of general uneasiness and unrest, and a fear lest I had taken an overdose. I now constantly walked about the house, my skin to myself was warm, in fact my whole surface felt flushed; my mouth and throat were very dry; my legs put on a strange, foreign feeling, as though they were not a part of my body. I counted my pulse and found it 120, quite full and strong. A foreboding, an undefined, horrible fear, as of impending death, now commenced to creep over me; in haste I sent for Dr. H. Allen, and he being out, directly afterwards for Dr. Thomas. The curious sensations in my limbs increased. My legs felt as though they were waxen pillars beneath me. I remember feeling them with my hand and finding them, as I thought at least, very firm, the muscles all in a state of tonic contraction. About 8 o'clock, I began to have marked “spells”—periods when all connection seemed to be severed between the external world and myself. I might be said to have been unconscious during these times, in so far that I was oblivious to all external objects, but on coming out of one, it was not a blank, dreamless void upon which I looked back, a mere empty space, but rather a period of active but aimless life. I do not think there was any connected thought in them; they seemed simply wild reveries, without any binding cord; each a mere chaos of disjointed ideas. The mind seemed freed from all its ordinary laws of association so that it passed from idea to idea, as it were, perfectly at random.

The duration of these spells to me was very great, although they really lasted but from a few seconds to a minute or two. Indeed I now entirely lost my power of measuring time. Seconds seemed hours; minutes seemed days; hours seemed infinite. Still I was perfectly conscious during the intermissions between the paroxysms. I would look at my watch, and then after an hour or two, as I thought, would look again and

find that scarcely five minutes had elapsed. I would gaze at its face in deep disgust, the minute hand seemingly motionless as though graven in the face itself; the laggard second hand moving slowly, so slowly. It appeared a hopeless task to watch during its whole infinite round of a minute, and always would I give up in despair before the 60 seconds had elapsed. Occasionally, when my mind was most lucid, there was in it a sort of duplex action in regard to the duration of time. I would think to myself it has been so long since a certain event, an hour for example, since the doctor came, and then reason would say, no it has been only a few minutes, your thoughts or feelings are caused by the hemp. Nevertheless I was not able to shake off this sense of the almost indefinite prolongation of time, even for a minute. The paroxysms already alluded to, were not accompanied with muscular relaxation. About quarter before 9 o'clock, I was standing at the door, anxiously watching for the doctor, and when the spells would come on I would remain standing, leaning slightly, perhaps, against the doorway. After awhile, I saw a man approaching, whom I took to be the doctor. The sounds of his steps told me he was walking very rapidly, and he was under a gas lamp, not more than one-fourth of a square distant, yet he appeared a vast distance away and a corresponding time approaching. This was the only occasion, in which I noticed an exaggeration of distance; in the room it was not perceptible. My extremities now began to grow cold and I went into the house. I do not remember further, until I was aroused by Dr. Thomas shaking or calling me. Then intellection seemed pretty good. I narrated what I had done and suffered, and told the doctor my opinion was, that an emetic was indicated both to remove any of the extract still remaining in my stomach and also to arouse the nervous system. I further suggested our going into the office as more suitable than the parlor, where we then were. There was at this time a very marked sense of numbness in my limbs, and what the doctor said was a hard pinch, produced no pain. When I attempted to walk up stairs my legs seemed as though their lower halves were made of lead. After this there were no new symptoms, only an intensifying of those already mentioned. The periods of unconsciousness became at once longer and more frequent, and during their absence intellection was more imperfect, although when thoroughly roused, I thought I reasoned and judged clearly. The oppressive feeling of impending death became more intense. It was horrible. Each paroxysm would seem to have been the longest I had suffered: as I came out of it, a voice seemed constantly saying, "you are getting worse—your paroxysms are growing longer and deeper—they will overmaster you—you will die."

A sense of personal antagonism between my will power and myself, as affected by the drug, grew very strong. I felt as though my only chance was to struggle against these paroxysms; that I must constantly arouse myself by an effort of will, and that effort was made with infinite toil and pain. I felt as if some evil spirit had control of the whole of me, except the will power, and was in determined conflict with that, the last citadel of my being. I have never experienced anything like the fearful sense of almost hopeless anguish and utter weariness which was upon me.

Once or twice during a paroxysm, I had what might be called night-mare sensations; I felt myself mounting upwards, expanding, dilating, dissolving into the wide confines of space, overwhelmed by a horrible, rending, unutterable despair. Then with tremendous effort, I seemed to shake this off, and to start up with the shuddering thought, next time you will not be able to throw this off, and what then! Under the influence of an emetic I vomited freely without nausea and without much relief. About midnight, at the suggestion of the doctors, I went up stairs to bed. My legs and feet seemed so heavy I could scarcely move them, and it was as much as I could do to walk with help. I have no recollection, whatever, of being undressed, but am told I went immediately to sleep. When I awoke early in the morning, my mind was at first clear, but in a few minutes the paroxysms, similar to those of the evening, came on again, and recurred at more or less brief intervals until late in the afternoon. All of the day there was marked anæsthesia of the skin.

At no time were there any aphrodisiac feelings produced. There was a marked increase of the urinary secretion. There were no after effects, such as nausea, headache, or constipation of the bowels.

The following notes were kindly furnished by Dr. Thomas: "I was called at 8½ p. m. to Dr. H. C. Wood, and was informed he had taken an over-dose of extract-cannab. indic. I found him presenting at first glance, the mental condition and excited manner of mild alcoholic intoxication. His powers of ratiocination were but slightly impaired. The most prominent psychological manifestation was a constant and overwhelming dread of impending death, which no amount of assurance could relieve for more than an instant; with this was combined an almost entire loss of the faculty of appreciating time—moments seeming to his disturbed consciousness to be hours in length. He stood and walked without difficulty, and his voice was natural in tone and accent. Pupils widely though not completely dilated; pulse moderately full, and numbering 106 beats per minute, increasing in frequency to 118 per minute within the following twenty minutes and becoming decidedly weaker. The extremities were cool and growing colder. Zinci Sulph. was now ordered with the view of evacuating the stomach of any of the drug which might remain unabsorbed, as well as for any possible revulsive influence it might exert. At ten minutes after 9, when the emetic was obtained, the pulse was found to have increased in frequency still farther (136) and to have proportionately decreased in volume. Within 15 minutes following, the feet meantime having been soaked in hot mustard water, free emesis took place, and the pulse rapidly fell, improving at the same time in quality. At 10.15 it was 104 per minute, and it remained about the same for the succeeding hour. The warmth of skin was at this time restored. The mental state varied but little throughout. At 11.15 I resigned the case to Dr. Allen."

The foregoing experiment proves that the Kentucky hemp does contain an appreciable quantity of the resinous active principle or principles, but it was merely tentative, and was not intended to determine the proportionate amount.

In order to determine the proportion of extract obtainable, the following experiment was performed:

Six ounces of the dried leaves of male Kentucky hemp plants were treated with hot alcohol and then exhausted with a little ether. The tinctures thus obtained were mixed and evaporated. The extract thus procured weighed 252 grains. One drachm of it was rubbed up with a strong solution of the Carbonate of Soda to remove fatty matters, &c. It lost nineteen grains or 32 per cent., very nearly one-third of its weight. Six ounces of the leaves, therefore, yielded rather more than two and two-thirds drachms of an extract, from which every thing soluble in an alkaline solution had been removed. The method employed resembles that of the Messrs. Smith of Edinburgh. They obtained from 6 to 7 per cent. of their purified extract from the plant grown in India. I obtained 4 to 5 per cent. of the extractive, and as the operation was on a small scale and conducted by one totally unversed in practical pharmacy, there can be no doubt that there was sufficient loss to bring up the proportion fully to 5 per cent.; moreover the American leaves were probably not so thoroughly dried as the Indian.

The therapeutic powers of this extract were not tested.

To test the matter further, I exhausted three ounces avoirdupois with hot alcohol, and the resultant tincture was placed in the hands of Hance, Griffith and Company, Manufacturing Chemists of this city.* Four-fifths of this tincture were evaporated by them to the consistency of a syrup, and to it was added ten times its bulk of water. The precipitate was washed and dried. When given into my hands, it was a softish greenish, adhesive resin. Of this I took $\frac{3}{4}$ of a grain dissolved in a mixture of alcohol and ether. It produced marked cerebral disturbance amounting to a mild intoxication.

These symptoms were similar to those heretofore detailed, but very much milder. There were, however, no marked periods of unconsciousness, merely a feeling of hilarity and a total inability to fix the attention except for a very short period and also some prolongation of time.

Of this same resinous extract, my friend, Carl Früh, a graduate of the Philadelphia College of Pharmacy, took one grain. He first felt the influence of it about supper time. His head felt as if some one was violently compressing it and at the same time there was a feeling of hilarity, with an uncontrollable desire to talk and laugh, so that those around him asked him what had come over him.

At supper he was almost ravenous and ate so much that it was noticed by others. Upon attempting to concentrate his thoughts upon any subject, he found it required a very painful effort. In attempting to compound a prescription, he found it impossible to remember more than one ingredient at a time, and even this was almost beyond his powers. In the evening he went to a lecture at the College of Pharmacy. Although he understood all that was said, yet he could not remember it a moment, and at times would forget his surroundings and then suddenly wake up to find himself sitting in the lecture room. Later in the evening he attended a society-meeting, and afterwards went out with a fellow student, but has no recollection of what was said or done. There was a good deal of pria-

*Now Hance, Brothers and White.

pism during the night, and a state of venereal excitement was induced, lasting several days. During the night, urine was passed very freely. Before this, he had taken two grains of Herring's extract with the result of producing similar symptoms, which were, however, no more intense than those caused by the single grain of the American resin.

Messrs. Hance and Griffith prepared the resin from the remainder of the hemp tincture, by first agitating with milk of lime, filtering, precipitating by sulphuric acid, agitating with animal charcoal, again filtering, concentrating by evaporation, and precipitating the resin by the addition of twice the bulk of water. The resin thus obtained was tested by my friend, Dr. Richardson, in the Pennsylvania Hospital, by permission of Dr. Da Costa, the attending physician. One-fourth of a grain of it was found to be sufficient to produce decided therapeutic results; in some cases acting very pleasantly as a hypnotic and calmative; in others, causing evident sensorial disturbance, but rather aggravating than alleviating the distress of the patient.

Having at that time a lady under my care, subject to severe attacks of neuralgia, I supplied her with some of the drug in $\frac{1}{4}$ grain pills. Of these she found one was always sufficient to induce a quiet sleep of some hours duration, from which she generally awoke free from pain. After the limited supply of this preparation was exhausted, I tried with her a similarly prepared extract made from imported India hemp plants, but a grain of this did not suffice to quiet the pain and induce sleep.

The above experiments are certainly sufficient to prove that the hemp plant, as grown in Kentucky, contains a sufficient abundance of the active principle, to be capable of yielding a supply to the pharmacist. If I am correctly informed, the India plant is worth at wholesale prices, about a dollar a pound in our market. The male seeding plants in Kentucky, after they have shed their pollen, are worthless. It was with such plants the experiments were instituted. A considerable supply of them might be obtained, so Mr. Hamilton writes me, for little more than the expense of gathering them, or if the demand should exceed the amount of such male plants, the leaves of the female plants when ready to be cut for the fibre might be obtained on the same terms.

A more important consideration than the mere monetary one, is the probability that, when the plants were raised near home, a more uniform product would be obtained.

There can be no doubt, that under certain circumstances cannabis indica supplies a medical need, which no other drug will so exactly meet. Yet, the extracts as kept in the shops, even when honestly made, vary so indefinitely in strength, and indeed are so generally almost inert, that the use of this narcotic has been largely abandoned in consequence. It is very probable that this variation depends to a certain extent upon differences in age and modes of cultivation, &c., of the plant. If this be so, the growth of the plant under the eye of the pharmacist will give him the opportunity of learning the conditions best fitted for developing in it the active principles.

The U. S. Pharmacopeia apparently recognizes the fact of the variance of the hemp extracts of commerce and directs a purified extract. The process of preparation given, consists simply of dissolving the crude extract in alcohol and evaporating. Unfortunately this does not meet the difficulty, since the solubility of the extract in alcohol is no certain measure of its activity. There are many inert matters existing in the plant which are soluble in alcohol, so that a fair amount of extract may be yielded by a specimen which contains almost no resin. This may occur to a certain extent even if India hemp plant be the subject of the trial and is very certainly the case when plants from other localities are employed.

In order to throw some light on this subject the following experiment was made : 100 grains of a fine looking extract made from India plants wholly soluble in alcohol, were rubbed up with a solution of potash, dissolved in alcohol, passed through animal charcoal precipitated by a strongly alkaline solution, filtered, and the resin carefully washed and dried. The resultant weighed 58 grains. Even if we allow as much as 12 per cent. for waste, there was, therefore, present in the original extract 30 per cent. of inert matters, which corresponds very closely with the amount of inert matter contained in the extract prepared by myself from the American plant. That the matters removed by potash are inert I proved in regard, at least to the American extract, by taking them in considerable amount without any perceptible effects being induced. In view of the above mentioned facts, it would seem advisable to replace in the U. S. Pharmacopeia for 1870, the present *Extractum cannabis purificatum* by a preparation to be called *Resina Cannabis*, and to be made by precipitating the concentrated tincture, by water rendered strongly alkaline by the presence of soda or potash.

Such a mode of preparing is essentially that originally published by the Messrs. Smith of Edinburg. The resin, as obtained by himself in this way, corresponds pretty closely with that described by the latter gentlemen in their original paper. It is fawn colored, in very thin layers, but when in mass, is blackish. It is neutral to test paper, and is apparently, a simple, active principle ; at least I have not been able to separate any organic principle from it. At one time, I strongly suspected the presence in it of an alkaloid, because its action on myself was so similar to that of the mydriatics.

In order to determine this point, a concentrated tincture was treated with water acidulated with acetic acid, filtered, and to the clear solution thus obtained an alkali was added, but no precipitate was afforded—neither did tannic acid produce any. This experiment was repeated, sulphuric acid being substituted for the acetic. The same negative result was obtained.

Again, a concentrated tincture was treated with freshly precipitated oxide of lead, filtered, the lead removed by the hydro-sulphate of ammonia and the water acidulated with sulphuric acid, was added. Upon again filtering, the clear solution obtained, did not respond to any of the tests for an alkaloid : dilute water of ammonia, filtered through the lead, gave no precipitate with muriatic acid, showing the absence of an insoluble organic acid.